



DYNC2H1 gene

dynein cytoplasmic 2 heavy chain 1

Normal Function

The *DYNC2H1* gene provides instructions for making a protein that is part of a group (complex) of proteins called dynein-2. The dynein-2 complex is found in cell structures known as cilia. Cilia are microscopic, finger-like projections that stick out from the surface of cells. Dynein-2 is involved in a process called intraflagellar transport (IFT), by which materials are carried within cilia. Specifically, dynein-2 is a motor that uses energy from the molecule ATP to power the transport of materials from the tip of cilia to the base.

IFT is essential for the assembly and maintenance of cilia. These cell structures play central roles in many different chemical signaling pathways, including a series of reactions called the Sonic Hedgehog pathway. These pathways are important for the growth and division (proliferation) and maturation (differentiation) of cells. In particular, Sonic Hedgehog appears to be essential for the proliferation and differentiation of cells that ultimately give rise to cartilage and bone.

Health Conditions Related to Genetic Changes

asphyxiating thoracic dystrophy

More than 50 mutations in the *DYNC2H1* gene have been identified in people with asphyxiating thoracic dystrophy, an inherited disorder of bone growth characterized by a small chest, short ribs, and shortened bones in the arms and legs. Mutations in this gene account for up to half of all cases of this condition. Most of the known mutations change single protein building blocks (amino acids) in the DYNC2H1 protein. The dynein-2 complex made with the altered protein cannot function normally, which disrupts IFT from the tip of cilia to the base and causes a buildup of materials at the tip. Researchers speculate that these changes in IFT alter certain signaling pathways, including the Sonic Hedgehog pathway, which may underlie the abnormalities of bone growth characteristic of asphyxiating thoracic dystrophy.

In some affected individuals, asphyxiating thoracic dystrophy is also associated with abnormalities of the kidneys, liver, retinas, and other tissues. However, when the disorder results from *DYNC2H1* gene mutations, its features are usually limited to problems with bone growth. The reasons for this difference are unknown.

other disorders

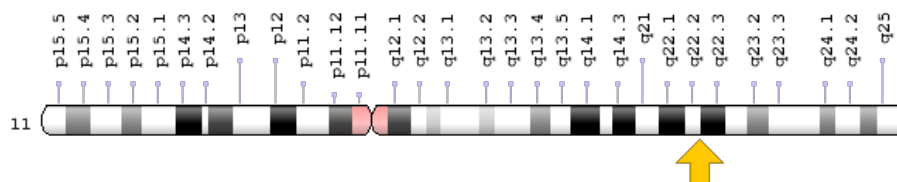
Mutations in the *DYNC2H1* gene have also been found to cause two other disorders of bone growth: short-rib polydactyly syndrome type II (SRPS type II), also known as Majewski syndrome, and short-rib polydactyly syndrome type III (SRPS type III), also known as Verma-Naumoff syndrome or Saldino-Noonan syndrome. These disorders have signs and symptoms similar to those of asphyxiating thoracic dystrophy, including a narrow chest and short ribs. However, SRPS type II and type III tend to be more severe than asphyxiating thoracic dystrophy, and affected individuals usually die before or shortly after birth.

About 10 *DYNC2H1* gene mutations have been identified in people with SRPS type II, and at least 4 mutations have been found in people with SRPS type III. Like the mutations that cause asphyxiating thoracic dystrophy, these genetic changes impair the function of the dynein-2 complex and disrupt IFT within cilia. Although the mechanisms seem to be similar, it is unclear why the effects of some *DYNC2H1* gene mutations are more severe than others. The mutations that cause SRPS type II and type III may impact protein function more severely than those that cause asphyxiating thoracic dystrophy.

Chromosomal Location

Cytogenetic Location: 11q22.3, which is the long (q) arm of chromosome 11 at position 22.3

Molecular Location: base pairs 103,109,431 to 103,479,863 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DHC1b
- DHC2
- DYH1B

- dynein, cytoplasmic 2, heavy chain 1
- hdhc11

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Cilia and Flagella Are Motile Structures Built from Microtubules and Dyneins
<https://www.ncbi.nlm.nih.gov/books/NBK26888/#A3075>
- Molecular Cell Biology (fourth edition, 2000): Cilia and Flagella: Structure and Movement
<https://www.ncbi.nlm.nih.gov/books/NBK21698/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28DYNC2H1%5BTI%5D%29>

OMIM

- DYNEIN, CYTOPLASMIC 2, HEAVY CHAIN 1
<http://omim.org/entry/603297>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_DYNC2H1.html
- HGNC Gene Family: Dyneins, cytoplasmic
<http://www.genenames.org/cgi-bin/genefamilies/set/538>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=2962
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/79659>
- UniProt
<http://www.uniprot.org/uniprot/Q8NCM8>

Sources for This Summary

- OMIM: DYNEIN, CYTOPLASMIC 2, HEAVY CHAIN 1
<http://omim.org/entry/603297>
- Dagoneau N, Goulet M, Geneviève D, Sznajder Y, Martinovic J, Smithson S, Huber C, Baujat G, Flori E, Tecco L, Cavalcanti D, Delezoide AL, Serre V, Le Merrer M, Munnich A, Cormier-Daire V. DYNC2H1 mutations cause asphyxiating thoracic dystrophy and short rib-polydactyly syndrome, type III. *Am J Hum Genet.* 2009 May;84(5):706-11. doi: 10.1016/j.ajhg.2009.04.016.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19442771>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2681009/>
- El Hokayem J, Huber C, Couvé A, Aziza J, Baujat G, Bouvier R, Cavalcanti DP, Collins FA, Cordier MP, Delezoide AL, Gonzales M, Johnson D, Le Merrer M, Levy-Mozziconacci A, Loget P, Martin-Coignard D, Martinovic J, Mortier GR, Perez MJ, Roume J, Scarano G, Munnich A, Cormier-Daire V. NEK1 and DYNC2H1 are both involved in short rib polydactyly Majewski type but not in Beemer Langer cases. *J Med Genet.* 2012 Apr;49(4):227-33. doi: 10.1136/jmedgenet-2011-100717.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22499340>
- Merrill AE, Merriman B, Farrington-Rock C, Camacho N, Sebald ET, Funari VA, Schibler MJ, Firestein MH, Cohn ZA, Priore MA, Thompson AK, Rimoin DL, Nelson SF, Cohn DH, Krakow D. Ciliary abnormalities due to defects in the retrograde transport protein DYNC2H1 in short-rib polydactyly syndrome. *Am J Hum Genet.* 2009 Apr;84(4):542-9. doi: 10.1016/j.ajhg.2009.03.015.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19361615>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2667993/>
- Okamoto T, Nagaya K, Kawata Y, Asai H, Tsuchida E, Nohara F, Okajima K, Azuma H. Novel compound heterozygous mutations in DYNC2H1 in a patient with severe short-rib polydactyly syndrome type III phenotype. *Congenit Anom (Kyoto).* 2015 Aug;55(3):155-7. doi: 10.1111/cga.12098.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/25410398>
- Schmidts M, Arts HH, Bongers EM, Yap Z, Oud MM, Antony D, Duijkers L, Emes RD, Stalker J, Yntema JB, Plagnol V, Hoischen A, Gilissen C, Forsythe E, Lausch E, Veltman JA, Roeleveld N, Superti-Furga A, Kutkowska-Kazmierczak A, Kamsteeg EJ, Elçioglu N, van Maarle MC, Graul-Neumann LM, Devriendt K, Smithson SF, Wellesley D, Verbeek NE, Hennekam RC, Kayserili H, Scambler PJ, Beales PL; UK10K, Knoers NV, Roepman R, Mitchison HM. Exome sequencing identifies DYNC2H1 mutations as a common cause of asphyxiating thoracic dystrophy (Jeune syndrome) without major polydactyly, renal or retinal involvement. *J Med Genet.* 2013 May;50(5):309-23. doi: 10.1136/jmedgenet-2012-101284. Epub 2013 Mar 1.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23456818>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3627132/>

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